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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 09/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/663,002	MUKHERJEE ET AL.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *6-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/18/2003, 3/17/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-16 are pending in the instant application.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-5) in the reply filed on 6/29/2006 is acknowledged.

Claims 6-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/29/2009.

An examination on the merits of claims 1-5 follows.

Information Disclosure Statement

Receipt of information disclosure statements, filed on 12/18/2003 and 3/17/2005, is acknowledged. The signed and initialed PTO 1449s have been mailed with this action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in that the metes and bounds of the phrase "suspected to bind" are unclear. The metes and bounds of the phrase are unclear in that what one suspects will bind another may not. Thus, the phrase is subjective and it is unclear as to how it limits the structure of the test compound. Further, the metes and bounds of the phrase "measuring a second level of mRNA transcript of the PPAR responsive gene formed in the cell is unclear." The phrase is unclear in that it could be referring to a repeat measurement of the mRNA transcript determined in the cell in step (a) or it could be referring to the determination of mRNA transcript in cell contacted with the test compound after the contacting has occurred. Method step (c) does not clearly relate back to method step (b). Moreover, it is unclear if the mRNA is measured in the same cell in parts (a) and (c), since the claim only refers to "the cell", which appears to be a single cell (and not a control cell and a test cell, for example). Accordingly, the metes and bounds of the claimed method are unclear.

Claims 2-5 depend from claim 1 and are indefinite for the same reasons as applied to claim 1.

Claim 4 is vague and indefinite in that the metes and bounds of the term "human proximal tubule derived cell (HK-2) are unclear. It is unclear if the human proximal tubule derived cell is limited to the HK-2 cell line or if the cell line is used only as an example of a proximal tubule derived cell. It would be remedial to amend the claim language to clearly indicate the metes and bounds of the cell encompassed by the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to the measurement of a "PPAR responsive gene" in any type of cell obtained from any species of organism. Claim 2 further limits the isoform of PPAR to PPAR-α, PPAR-β(δ), or PPAR-γ, but does not limit the type of cell or organism. Claim 3 limits the cell to a mammalian cell but does not specify the type of cell. Claim 4 further limits the mammalian cell to a human proximal tubule derived cell (HK-2). Claims 3 and 4 do not limit the gene assayed or isoform of PPAR. Claim 5 is drawn to the measurement of pyruvate dehydrogenase kinse-4 (PDK-4) or adipocyte differentiation relating protein (ADRP) from any species. Thus, the claims encompass a set of PPAR-α, responsive genes from any organism and any cell type, PPAR-β(δ) responsive genes from any organism and any cell type, or PPAR-γ responsive genes from any organism and any cell type. Further, the claims encompass any PPAR responsive gene present in a human proximal tubule derived cell. Moreover, the claims encompass any PDK-4 or ADRP gene from any organism and cell type. Accordingly, the claims encompass a large genus of PPAR responsive genes.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or

chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification teaches that there are species differences and cell type differences in the expression of PPAR responsive genes (e.g. page 2, lines 15-32; page 3, lines 4-7; page 10, lines 20-24; paragraph bridging pages 11-12; Figure 1B). The specification describes PDK-4 and ADRP as PPAR responsive genes in human HK-2 cells (e.g. page 3, lines 23-26; Figures 1A and 2A). PDK-4 is further classified as a PPAR responsive gene in hamster kidney and hamster liver (e.g. page 3, lines 26-32; Figure 4). However, increased PDK-4 and ADRP expression was not consistent among all cell lines tested: HK-2, SW872, LNCaP, ACHN, HepG2 and Caki-1 (e.g. paragraph bridging pages 11-12; Figure 1B). Given the variability seen between species and cell types, the disclosure of PDK-4 as a PPAR responsive gene in human HK-2 cells and hamster kidney and liver cells and of ADRP as a PPAR responsive gene in human HK-2 cells, there is not a significant structure/function correlation that would allow one to use PDK-4 and/or ADRP in a representative number of species and cell types encompassed by the claims.

Even if one accepts that the examples described in the specification meet the claim limitations of the rejected claims with regard to structure and function, the examples are only representative of small set of genes that may be used in HK-2 cells or hamster liver or kidney. The results are not necessarily predictive of the ability to use these genes in other species or cell types. Thus, it is impossible for one to extrapolate from the few examples described herein those genes that would necessarily meet the structural/functional characteristics of the rejected claims.

The prior art does not appear to offset the deficiencies of the instant specification in that it does not describe a representative number of PPAR responsive genes for each of the PPAR

isoforms, species and cell types encompassed by the claims. For example, Way et al (Endocrinology, Vol. 142, No. 3, pages 1269-1277, March 2001) teach genes that are up- or down-regulated in response to PPARγ activation in rat (e.g. Table 2). However, the genes are not consistently regulated across all cell types (e.g. Table 2). This lack of structure function correlation requires the identity of PPAR responsive genes to be experimentally determined for each condition: PPAR isoform (α, β(δ) and γ), organism (e.g. Drosophila, C. elegans, cow, pig, rat, mouse, human, etc.) and cell type (e.g. fibroblast, muscle, hepatocyte, kidney epithelial cell, neuron, etc.).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states, "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of PPAR responsive genes, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to

lack of written description for that broad class. The specification provided only the bovine sequence.

Given the very large genus of PPAR responsive genes encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to the specific PPAR responsive genes for each isoform and a representative number of organisms and cell types, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus of PPAR responsive genes. Thus, there is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those PPAR responsive genes that satisfy the functional limitations of the claims. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 1-5.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Way et al (Endocrinology, Vol. 142, No. 3, pages 1269-1277, March 2001; see the entire reference).

Regarding claim 1, Way et al teach a method comprising the steps of (i) treating ZDF rats for 7 days with either GW1929 or vehicle alone, (ii) determining the level of a plurality of mRNA transcripts in cells exposed to GW1929 or vehicle alone with GeneCalling mRNA profiling technology, and comparing the level of transcripts in cells exposed to GW1929 and cells exposed to vehicle alone (e.g. paragraph bridging pages 1270-1271). GW1929 is a tyrosine-based PPARγ agonist (e.g. paragraph bridging pages 1270-1271). The genes that are upregulated or downregulated by GW1929 and are thus PPARγ responsive genes are disclosed in Table 2 (page 1272).

Regarding claim 2, Way et al teach that GW1929 is a selective PPARγ modulator (e.g. paragraph bridging pages 1269-1270).

Regarding claim 3, Way et al teach the method in rat cells, which are mammalian cells.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Jiang et al (Journal of Lipid Research, Vol. 42, pages 716-724, May 2001; see the entire reference).

Regarding claim 1, Jiang et al teach a method comprising culturing SW cells in the presence of clofibrate for 0-72 h, isolating mRNA for $cPLA_2$ and COX-2, determining the level of $cPLA_2$ and COX-2 mRNA at various time intervals, including 0 and 72 h, and comparing the amount of mRNA at each of the time intervals (e.g. page 720, Up-regulation of $cPLA_2$ and COX-2 mRNA by clofibrate; Figures 3 and 4).

Regarding claim 2, Clofibrate is a known PPARα agonist (e.g. page 722, right column, 1st full paragraph).

Regarding claim 3, the SW cells used by Jiang et al are preadipocyte SW 872 (SW) cells, derived from human liposarcoma and are thus mammalian cells (e.g. page 717, Cell culture and radiolabeling).

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Crabb et al (Alcoholism: Clinical and Experimental Research, Vol. 25, No. 7, pages 945-952, July 2001; see the entire reference).

Regarding claim 1, Crabb et al teach a method comprising treating rats with and without clofibrate, measuring the level of *ALDH2* mRNA expression in rats with and without treatment with clofibrate, and comparing the levels of ALDH2 mRNA expression (e.g. page 949, *Effect of Clofibrate Treatment on ALDH2 Expression in Rat Liver*).

Regarding claim 2, Crabb et al teach the analysis of PPARα (e.g. page 949, *Effect of Clofibrate Treatment on ALDH2 Expression in Rat Liver*).

Regarding claim 3, the cells used in the method of Crabb et al are rat cells and are thus mammalian cells (e.g. page 949, *Effect of Clofibrate Treatment on ALDH2 Expression in Rat Liver*).

Claims 1-3 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Wu et al (Diabetes, Vol. 48, pages 1593-1599, August 1999; see the entire reference).

Regarding claim 1, Wu et al teach a method comprising treating rats with or without WY-14,643 for 3 days, measuring the level of PDK4 mRNA from cells with and without WY-14,643 treatment, and comparing the levels of mRNA between treated and untreated cells to determine

that WY-14,643 increases PDK4 mRNA expression (e.g. page 1596, left column, 1st full paragraph; Figure 5).

Regarding claim 2, Wu et al teach that WY-14,643 is a PPARα agonist (e.g. page 1598, left column, 2nd full paragraph).

Regarding claim 3, Wu et al teach the use of cells obtained from rat (i.e. a mammal) (e.g. page 1596, left column, 1st full paragraph; Figure 5).

Regarding claim 5, Wu et al teach the measurement of PKD4 mRNA (e.g. page 1596, left column, 1st full paragraph; Figure 5).

Examiner Note

Human cell line HK-2 is available from ATCC as ATCC® Number: CRL-2190™.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

CELINE QIAN, PH.D
PRIMARY EXAMINER

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Dunston, Ph.D.
Examiner
Art Unit 1636

jad